The claims have now been limited to secretory leucocyte protease inhibitor which is not disclosed in any of the cited reference. Moreover, none of the references relate to a collagen related disease.

The present claims have been presented so as to limit the issues and are not intended to admit that the cited art is pertinent as to alpha1-antitrypsin or alpha2-macroglobulin. The cited art relates to the treatment of inflammatory conditions where mast cells are involved. This is not the case here. As noted in the preamble of claim 21, there is provided the treatment of a collagen related autoimmune arthritis.

The Rejection Under 35 USC 103(a)

Reconsideration is respectfully requested of the rejection of the claims as now presented as being unpatentable over WO 00/51623 or Patent No. 5114917 in view of U.S. Patent No. 4496689 and WO 99/55310.

The present claims relate to the treatment of collagen related autoimmune disease rheumatoid arthritis. As previously noted from the Merck Manual, rheumatoid arthritis is present in two different forms. One form is the type characterized by inflammation and the degrannulation of mast cells which relates to the prior art. In collagen related autoimmune arthritis, the inflammation is gone and there are autoantibodies circulating throughout the body as well as compliment components and collagenase which participate in the pathogenesis of erosive arthritis. It is known that members of the complement network (the alternative pathway and C5a) and cytokines (interleukin-1), TNF-α as well as neutrophiles have essential roles. The antibodies cause the release of TNF-α. The circulation causes an attack on other joints in the body and not only the joint which is initially inflamed. It is known that secretory leucocyte protease inhibitor binds

with antibodies, TNF-α, and collagenase. However, the drug, when administered orally circulates through the body and binds with the factors causing the nodules and deformation of fungas. The steroid is used to bind with interleukin-1.

WO '623 relates only to alpha1-antitrypsin.

Secretory leucocyte protease inhibitor is structurally distinct from alpha1-antitrypsin. It is a small molecule but has active binding sites. Its similarity to alpha1-antitrypsin is its binding sites and not its chemical configuration. The present inventors were the first to recognize the use as an anti-collagenase. The references are silent with regard to collagen related diseases.

Mitra discloses a complex of alpha1-antitrypsin only and the use is for pulmonary emphysema which is a result of a hereditary deficiency. The administration is only intravenously (col. 9, lines 13 and 14).

Lezdey '917 relates primarily to alpha1-antitrychymotrypsin as an anti-inflammatory agent. Alpha1-antitrypsin is also noted but not for reason that it is anticollagenase. The reference is silent with regard to secretory leucocyte protease inhibitor and collagen related diseases.

WO 99/55310 does not relate to secretory leucocyte protease inhibitor or to treatment of a collagen related disease.

Lapin is not at all pertinent to the presently claimed invention. The reference is directed to treating inflammatory arthritis with anti-inflammatory agents which are not proteins. A steroid is used in the present invention to bind with interleukin-1 and not to shut down an inflammatory cascade.

The claims now presented provide multiple distinctions over the cited art. None relate to secretory leucocyte protease inhibitor or any of the pro-drugs which are intended to provide controlled delivery in the small intestine, the preferred site of absorption for many drugs.

The preamble provides a further distinction.

Applicants' position that the preamble should also be considered in considering whether or not the invention is obvious is well supported by the legal authorities: In In re Szanhan and Lump, 164, USPQ 632, (CCPA 1970), the Court in reversing the Board of Appeals held the claims in issue to be patentable over the prior art (a 34 USC 103 rejection) because as the Court states in the "preamble of claims is more than a statement of intended use."

The pertinent portions of the Court's decision are reproduced below (as P. 635, 636, Emphasis supplied).

The Board also affirmed the rejection of claims 8, 9, and 16-18 as being unpatentable over Haines in view of Lawson, Graham, and Benson, specifically adding:

> "Haines show the advantage of convertibility of a smooth surface mold to one which can mark the bottle and both Graham et al and Benson show how a marking insert can be attached to a smooth molding surface at any location desired within the boundaries of that surface."
> Hence, while effectively admitting that the structural recitations in the claims in question find response in Frank, appellants point out that the reference relates to decorative indicia to be applied to packages, wrapping paper, etc. and it silent as to a mold insert, thus failing to render the claims obvious.

The court continued at page 636 as follows in response to the solicitor's argument that preambles should be denied the effect of a limitation:

"We are, however, inclined to agree with appellants under the circumstances here. The preamble appears to be more than a mere statement of intended use since it gives "life and meaning" to the recitation in the body of the claims referring to "configurated complementary to the desired molded surface" and "adhesives... for securing the insert within a mold."
Considering the introductory language as providing the setting or background for the words that follow...
(Emphasis applied, at p. 636)

The Court went on to point out that the prior art failed to suggest what was stated in the preamble. This is the same situation as here and the case is directly applicable to the issue presented here.

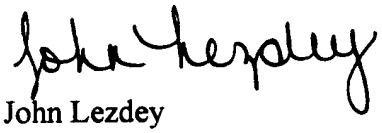
Conclusion

The present claim now sets forth several distinctions over the prior art:

1. The preamble and its recitation of collagen related diseases.
2. Secretory leucocyte protease inhibitor and its pro drug form.
3. Oral delivery for collagen related autoimmune disease.
4. Administration is not at the site of injury.

Reconsideration and favorable action are earnestly solicited.

Respectfully submitted,



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